Fetal surgical repair with placenta-derived mesenchymal stromal cell engineered patch in a rodent model of myelomeningocele.

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Public Summary:
Public Summary Purpose: Myelomeningocele (MMC), or spina bifida, is a neural tube defect that leads to paralysis, bladder incontinence and bowel dysfunction due to spinal cord injury. Fetal intervention provides coverage of the spinal cord to prevent further intrauterine damage; however it cannot reverse previously acquired damage. Our laboratory has demonstrated that placenta derived mesenchymal stromal cells (PMSCs) have the ability to help protect neurons and rescue motor function in a sheep model of MMC. The goal of this study was to determine the feasibility of fetal surgical repair of MMC in a rodent model using human PMSCs. Methods: Stem cells were isolated from second trimester placenta and seeded onto tissue patches (extracellular matrix). Fetal rodents with MMC underwent surgical repair using the stem cells and tissue patch. We tested various densities of stem cells. Fetal rodents were then delivered three days later. We measured the spinal cord and determined the number of apoptotic, or dead, cells. Results: 121 pups underwent MMC repair and 103 (85.1%) survived to delivery. Pups treated with the stem cells and tissue patch at all seeding densities resulted in significantly less cord compression compared to pups repaired with tissue patch only and unrepaired controls. Pups treated with the highest seeding density of PMSCs had significantly lower apoptotic cells compared to the tissue patch only. Conclusion: Surgical repair of MMC with stem cells on a tissue patch is feasible with a survival rate of 85.1%. Fetal rodents repaired with stem cells and a tissue patch have significantly less cord deformity and decreased evidence of apoptosis compared to the tissue patch only controls. This indicates that PMSCs may be capable of enhancing fetal wound healing and remodeling of the MMC spinal cord.

Scientific Abstract:
PURPOSE: The purpose of this study is to determine the feasibility of fetal surgical repair of myelomeningocele (MMC) in a rodent model using human placental mesenchymal stromal cells (PMSCs) seeded onto extracellular matrix (ECM) and to characterize the resulting changes in spinal cord tissue. METHODS: Fetal rodents with retinoic acid (RA) induced MMC underwent surgical repair of the MMC defect using an ECM patch on embryonic age (EA) 19 and were collected via caesarean section on EA 21. Various seeding densities of PMSC-ECM and ECM only controls were evaluated. Cross-sectional compression (width/height) and apoptotic cell density of the lumbosacral spinal cord were analyzed. RESULTS: 67 dams treated with 40mg/kg of RA resulted in 352 pups with MMC defects. 121 pups underwent MMC repair, and 105 (86.8%) survived to term. Unrepaired MMC pups had significantly greater cord compression and apoptotic cell density compared to normal non-MMC pups. Pups treated with PMSC-ECM had significantly less cord compression and demonstrated a trend towards decreased apoptotic cell density compared to pups treated with ECM only. CONCLUSION: Surgical repair of MMC with a PMSC-seeded ECM disc is feasible with a postoperative survival rate of 86.8%. Fetal rodents repaired with PMSC-ECM have significantly less cord deformity and decreased histological evidence of apoptosis compared to ECM only controls.